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COMPARATIVE ANALYSIS OF THE ABILITY OF ETANERCEPT AND INFLIXIMAB TO LYSE TNF-EXPRESSING CELLS IN A COMPLEMENT DEPENDENT FASHION.

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Abstract 116

Published reports 2 have demonstrated that infliximab (REMICADE®), a mouse-human chimeric antibody to TNF, is able to kill some TNF-expressing cells *in vitro* in the presence of complement (C'). Those experiments utilized cells that were unable to shed TNF and thus expressed high levels of cell-surface TNF. We have examined the ability of etanercept (ENBREL®), a soluble fusion protein consisting of two human p75 TNF receptors linked to the Fc region of human IgG1, to kill TNF-expressing cells in the presence of C'. To directly assess the ability of etanercept to kill TNF-expressing cells, cDNAs containing the sequence for a mutated human TNF gene were obtained. The mutated genes encoded a sequence that greatly reduced the amount of TNF shed from the cell surface. These genes were transfected into CHO cells, and cell lines expressing high levels of cell surface TNF were generated following four sequential rounds of FACS staining and sorting with an anti-TNF monoclonal antibody. Etanercept and infliximab were equivalent in their ability to bind and neutralize the cell surface TNF as measured by FACS analysis and bioassay, respectively. As previously reported, infliximab was able to mediate complement-dependent killing of the TNF-expressing cells (60% lysis at 0.5 mg/mL). In contrast, etanercept was not able to mediate complement-dependent killing of the TNF-expressing cells (0% lysis at 1.0 mg/mL). The data highlight a unique difference between these TNF antagonists and suggests that etanercept and infliximab may have different mechanisms of action *in vivo*.

EXHIBIT N

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1. Reference not provided.

2. Scallon et al. Cytokine 7:251-259, 1995. [Context Link]

Section Description

Hall C Abstracts # 115 - 210

ACR Poster Session A

Health Services and Outcomes I

Sunday, November 14, 1999, 8:00 AM-9:30 AM

ACR Poster Session A

Cytokines and Mediators I

Sunday, November 14, 1999, 8:00 AM-9:30 AM

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